Appl. No. 10/773,761 Amdt. dated September 30, 2006 Reply to Office Action of June 1, 2006

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

- 1-5. (canceled)
- 6. (Currently amended) A method to determine the survival clinical outcome of a breast cancer afflicted subject if treated with tamoxifen or other an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cancer cells from said subject for the ratio of HoxB13 and IL17BR expression levels level(s) of one or more genes in Table 2 or 3.
- 7. (Currently amended) The method of claim 6 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis <u>or survival outcome</u>.
- 8. (Original) The method of claim 6 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).
- 9. (Original) The method of claim 6 wherein said sample of breast cancer cells is ER+.
- 10. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of nucleic acids prepared by mRNA amplification from said sample of breast cancer cells.

- 11. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of one or more genes HoxB13 and IL17BR comprises detection of nucleic acids from said sample of breast cancer cells by quantitative PCR.
- 12. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of <u>HoxB13</u> and <u>IL17BR</u> proteins encoded by said genes or proteolytic fragments of said proteins.
- 13. (Original) The method of claim 12 wherein said detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.
- 14. (Currently amended) A method of determining prognosis of a subject having breast cancer if treated with tamoxifen or another an antiestrogen agent against breast cancer, or of a subject afflicted with breast cancer and treated with tamoxifen or another an antiestrogen agent against breast cancer, said method comprising:

assaying for the <u>ratio of HoxB13 and IL17BR</u> expression <u>levels in</u> <u>level(s) of one or more</u> genes in <u>Table 2 or 3 from</u> a breast cancer cell sample from said subject.

- 15. (Currently amended) The method of claim 14 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis <u>or survival</u> outcome.
- 16. (Original) The method of claim 14 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).
- 17. (Original) The method of claim 14 wherein said sample of breast cancer cells is ER+.

- 18. (Currently amended) The method of claim 14 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of nucleic acids prepared by mRNA amplification from said sample of breast cancer cells.
- 19. (Currently amended) The method of claim 14 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of nucleic acids from said sample of breast cancer cells by quantitative PCR.
- 20. (Currently amended) The method of claim 14 wherein said assaying for the expression levels of one or more genes HoxB13 and IL17BR comprises detection of HoxB13 and IL17BR proteins encoded by said genes or proteolytic fragments of said proteins.
- 21. (Original) The method of claim 20 wherein said detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.
- 22. (Original) The method of claim 14 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.
- 23. (Currently amended) A method to determine therapeutic treatment for a breast cancer patient based upon said patient's expected response or lack of response to treatment with tamoxifen or another an antiestrogen agent against breast cancer, said method comprising

determining an expected response or non-response to treatment with tamoxifen or another an antiestrogen agent against breast cancer for said patient by assaying a sample of breast cancer cells from said patient for the ratio of HoxB13 and IL17BR expression levels according to claim 6 level(s) of one or more one genes in Table 2 or 3; and

selecting the appropriate treatment for a patient with such a survival clinical outcome.

- 24. (Currently amended) The method of claim 23 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis <u>or survival outcome</u>.
- 25. (Original) The method of claim 24 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).
- 26. (Original) The method of claim 24 wherein said sample of breast cancer cells is ER+.
- 27. (Currently amended) The method of claim 24 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of nucleic acids prepared by mRNA amplification from said sample of breast cancer cells.
- 28. (Currently amended) The method of claim 24 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of nucleic acids from said sample of breast cancer cells by quantitative PCR.
- 29. (Currently amended) The method of claim 24 wherein said assaying for the expression levels of one or more genes <u>HoxB13</u> and <u>IL17BR</u> comprises detection of <u>HoxB13</u> and <u>IL17BR</u> proteins encoded by said genes or proteolytic fragments of said proteins.
- 30. (Original) The method of claim 29 wherein said detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.
- 31. (Original) The method of claim 24 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.

32. (Currently amended) A method to determine the survival clinical outcome of a human subject having breast cancer if treated with tamoxifen or another an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cells from said subject for expression of one or more human HOXB13, IL17BR or CACNA1D HoxB13 or IL17BR sequences or optionally another sequence the expression of which is correlated with their expression in breast cancer cells,

wherein underexpression of HOXB13 sequences is indicative of responsiveness, and overexpression of IL17BR and/or CACNA1D sequences is indicative of non-responsiveness, to treatment with tamoxifen or another <u>an</u> antiestrogen agent against breast cancer.

- 33. (Original) The method of claim 32 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).
- 34. (Currently amended) The method of claim 32 wherein said sample of breast cancer cells is ER+ or is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.[[.]]
- 35. (Original) The method of claim 32 wherein said assaying for expression comprises detection of nucleic acids prepared by mRNA amplification from said sample of breast cancer cells or detection of nucleic acids from said sample of breast cancer cells by quantitative PCR.
- 36. (Currently amended) The method of claim 32 wherein said assaying for expression comprises detection of proteins encoded by said genes sequences or proteolytic fragments of said proteins.

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- 37. (Original) The method of claim 36 wherein said detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.
- 38. (Currently amended) The method of claim 32 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HOXB13, HL17BR or CACNA1D HoxB13 or IL17BR sequences.

39-41. (canceled)

42. (Currently amended) The method of claim 32 wherein said assaying for expression comprises assaying for inactivation or methylation of HOXB13, IL17BR or CACNA1D HoxB13 or IL17BR sequences.

43-48. (canceled)

- 49. (Currently amended) A method to determine the survival clinical outcome of a human subject having breast cancer if treated with tamoxifen or another an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cells from said subject for expression of an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, [[9, 11-17,]] or 32-34.
- 50. (Currently amended) A method to determine the survival clinical outcome of a human subject having breast cancer if treated with tamoxifen or another an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cells from said subject for expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37 18-31, or 35-37.

51. (canceled)

- 52. (New) The method of claim 14 wherein said assaying is for expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.
- 53. (New) The method of claim 14 wherein said assaying is for expression of an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, or 32-34.
- 54. (New) The method of claim 23 wherein said assaying is for expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.
- 55. (New) The method of claim 23 wherein said assaying is for expression of an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, or 32-34.
- 56. (New) The method of claim 32 wherein said assaying is for expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.
- 57. (New) The method of claim 32 wherein said assaying is for expression of an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, or 32-34.
- 58. (New) The method of claim 6 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.
- 59. (New) The method of claim 32 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis or survival outcome.
 - 60. (New) The method of claim 32 wherein said sample of breast cancer cells is ER+.
- 61. (New) The method of claim 6 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 or IL17BR sequences.

- 62. (New) The method of claim 14 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 or IL17BR sequences.
- 63. (New) The method of claim 23 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 or IL17BR sequences.
- 64. (New) The method of claim 6 wherein said assaying for expression comprises assaying for methylation of HoxB13 or IL17BR sequences.
- 65. (New) The method of claim 14 wherein said assaying for expression comprises assaying for methylation of HoxB13 or IL17BR sequences.
- 66. (New) The method of claim 23 wherein said assaying for expression comprises assaying for methylation of HoxB13 or IL17BR sequences.